

# Percutaneous cervical cordotomy for the control of pain in patients with pleural mesothelioma

M B Jackson, D Pounder, C Price, A W Matthews, E Neville

## Abstract

**Background**—Severe chest pain is common in mesothelioma. Percutaneous cervical cordotomy, which interrupts the spinothalamic tract at the C1/C2 level causing contralateral loss of pain sensation, is particularly appropriate in mesothelioma as the tumour is unilateral and systemic analgesia may be ineffective and is limited by harmful side effects.

**Method**—A retrospective review was performed to determine the effectiveness and complication rate of this procedure.

**Results**—Fifty two patients were using opioids prior to cordotomy. The median daily dose of morphine before and after cordotomy was 100 mg (range 0–1000 mg) and 20 mg (range 0–520 mg), respectively ( $p < 0.001$ ). Forty three patients (83%) had a reduction in pain such that their dose of opioid could be at least halved. Twenty patients (38%) were able to stop completely. Recurrence of pain requiring an increase in opioid medication was recorded in 18 patients at a median time of nine weeks (range 0.7–26 weeks). Four patients developed mild weakness, two had troublesome dysaesthesia. The median time from cordotomy to death was 13 weeks (range 0.3–52 weeks). Six early deaths within two weeks of cordotomy occurred early in the series and reflect postoperative chest infection and poor selection as the patients were in the terminal stages of mesothelioma.

**Conclusions**—Percutaneous cervical cordotomy is successful in treating pain from mesothelioma. There was a low complication rate in this series. Referral to a unit experienced in cordotomy is recommended as soon as pain from chest wall invasion is suspected.

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**Keywords:** cordotomy; pleural mesothelioma; pain control

Malignant mesothelioma is a tumour arising from mesothelial cells which occurs most commonly in the pleura. In most cases there is a history of exposure to asbestos which is causally related.<sup>1</sup> The incidence of malignant mesothelioma is still increasing and it is predicted that it will continue to do so into the early part of the next century.<sup>2</sup> It is a common condition in those geographical areas where there is a large population of dockyard workers who have been subjected to heavy asbestos exposure in the past. Severe intractable chest

pain, known as the costopleural syndrome,<sup>3,4</sup> is a common feature of pleural mesothelioma as the tumour often invades the pleural cavity and thoracic wall early in the disease process. In a survey of 200 patients pain was a presenting symptom in 58%.<sup>5</sup> Systemic analgesia is generally the first choice of treatment to relieve most cases of cancer pain; however, nociceptive pathway block should be considered early in the costopleural syndrome as systemic analgesia often fails to give sufficient relief.<sup>3,4</sup>

Surgical section of the anterolateral tract of the spinal cord in the treatment of persistent pain was described at the beginning of this century.<sup>6</sup> The technique has since been refined using electrode thermocoagulation. Percutaneous cervical cordotomy interrupts the spinothalamic tract at C1/2 by means of a controlled radiofrequency electric current, causing contralateral loss of pain sensation below the level of the lesion.<sup>7,8</sup> Complete lesion of the spinothalamic tract can render virtually one half of the body pain free. The technique of percutaneous cervical cordotomy is well described elsewhere.<sup>9</sup>

Percutaneous cervical cordotomy is well recognised for the treatment of the costopleural syndrome,<sup>3,10,11</sup> and may be particularly appropriate when this is caused by pleural mesothelioma. There is usually unilateral disease, but it is too diffuse to allow other more local nociceptive pathway blocks to be effective.

In this retrospective review we describe the use of percutaneous cervical cordotomy in the control of pain in 53 patients with malignant pleural mesothelioma, studying the effectiveness and complication rate of the procedure. Patients with pleural mesothelioma were selected for percutaneous cervical cordotomy when they developed pain due to chest wall invasion. Inevitably this meant that the patient had started opioid medication, usually in combination with a non-steroidal anti-inflammatory drug, as simple analgesia alone had by this stage proved ineffective in obtaining pain control. After effective cordotomy the dose of opioid is halved to prevent respiratory depression. Further reductions can be made more slowly over the ensuing two weeks to prevent withdrawal symptoms.

## Methods

A retrospective review was performed of all available notes of patients who had undergone cordotomy for pain from pleural mesothelioma since 1985. Where data collection was incomplete, information was sought by letter to the patient's general practitioner. To increase objectivity the information was obtained and

Department of  
Respiratory Medicine  
M B Jackson  
A W Matthews  
E Neville

Department of Pain  
Control  
D Pounder  
C Price

Portsmouth Hospitals  
NHS Trust,  
Portsmouth, UK

Correspondence to:  
Dr M B Jackson,  
Department of Respiratory  
Medicine, Southampton  
General Hospital,  
Southampton SO16 6YD,  
UK.

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evaluated by one of us (MBJ) who was not involved with the work of the Pain Clinic.

## Results

The records of 53 patients (52 men) were obtained. Data on opioid dose were available at least until two weeks after the procedure (or until death if this occurred sooner) in 52 patients (98%). Information was requested from the patient's general practitioner in five cases and the date of death was subsequently obtained in four instances. The median age at the time of cordotomy was 64 years (range 44–82). The median time from the diagnosis of pleural mesothelioma to cordotomy was 21 weeks (range three days to 143 weeks). The median time from diagnosis to death in 51 patients was 24 weeks (range 10 days to 164 weeks). At the time of presentation 40 patients (75%) had a pleural effusion, eight (15%) had a pleural mass/thickening, and one patient had pleural encasement by tumour. The type of pleural involvement was not clear from the case notes in the remaining four patients (8%).

## PAIN RELIEF

Forty eight of the 53 patients (91%) were taking controlled release morphine sulphate tablets, often in conjunction with morphine elixir as required. Seven patients (13%) were using a diamorphine infusion. Only one patient was not taking either of these drugs at the time of cordotomy, as they had caused troublesome side effects previously. There is no direct equation defining the relationship between equivalent doses of oral morphine and subcutaneous diamorphine but, for the purposes of this analysis, we have used an equivalence used commonly in palliative care.<sup>12</sup>

Thirty six of the 53 patients (68%) had taken or were taking co-analgesic medication in addition to morphine/diamorphine. The most frequently used were non-steroidal, anti-inflammatory drugs, which had been taken by 31 patients (58%).

After percutaneous cervical cordotomy 20 patients (38%) were able to stop taking morphine/diamorphine completely. A further 19 (37%) continued on regular opioid medication but at less than half of the dose prior to the procedure. Overall, in 43 of 52 patients (83%) there was an improvement in pain, allowing a 50% or greater reduction in opioid dose.

The median daily dose of morphine before cordotomy was 100 mg (range 0–1000 mg) and the median lowest daily dose of morphine after cordotomy was 20 mg (range 0–520 mg),  $p < 0.001$  (Mann-Whitney test). After percutaneous cervical cordotomy, co-analgesic medication was continued in 18 patients (34%), eight of whom were managed solely on a non-steroidal anti-inflammatory drug and 10 on a combination of non-steroidal anti-inflammatory drug with either morphine or carbamazepine. Twenty three patients (43%) were not taking co-analgesic medication after cordotomy. This had been discontinued in seven patients after a successful procedure, and in the other patients had been considered

unhelpful prior to the procedure. In the remaining 12 patients it was not clear from the case records whether co-analgesic medication had been prescribed after percutaneous cervical cordotomy.

Four of the 53 patients (8%) proceeded to a second cordotomy because of initial failure in producing adequate relief, and this was successful in three instances.

Recurrence of severe pain requiring a subsequent increase of opioid was noted in 18 patients (34%). The median time for this recurrence in the 14 case notes in which it was recorded was nine weeks (range five days to six months).

## COMPLICATIONS

Two patients experienced troublesome dysaesthesia following cervical cordotomy and persistent motor weakness was noted in four. This was only graded in one patient (4/5, Medical Research Council scale for grading muscle function), although in the other three it was not regarded as severe. No patient suffered hemiplegia or was unable to walk as a result of their weakness. Unfortunately no data were found on the duration of this weakness in any patient.

The median time from cordotomy to death in 51 patients was 13 weeks (range two days to 52 weeks). Three patients (6%) died within one week of cordotomy and there were three other early deaths within two weeks of the procedure. In terms of pain control, the procedure had been a success in five of these patients and none had needed a second procedure to achieve a satisfactory result. Two of these patients were severely disabled by dyspnoea at rest because of pleural encasement from their tumours, and the third patient had marked cachexia and a very short life expectancy due to the mesothelioma itself. Two of the other patients who died early developed evidence of a chest infection following cordotomy, with pyrexia and a cough productive of green sputum. No information was available regarding the sequence of events leading to death in the sixth patient.

There were no other complications recorded. In particular, no patient developed incontinence due to sphincter disturbance. Impotence and postural hypotension can be expected in bilateral cordotomy (which this unit does not practise because of the higher incidence of central sleep apnoea, the "Ondine syndrome"<sup>13 14</sup>), but are usually rare in unilateral cordotomy and were not recorded.

## Discussion

It can be inferred that most of the patients in this series (83%) had a significant reduction in pain, and 20 of 52 (38%) were able to stop opioid medication completely. This is an important finding in pleural mesothelioma as the pain is often severe and opioid resistant. This is a retrospective review, however, with all the problems inherent therein. Some data were difficult to confirm because we can only be sure of relevant data that were recorded in the individual case notes. In particular, the lowest dose of morphine following the procedure, the use

of co-analgesic medication, the recurrence of pain, and the incidence of minor complications may not have been recorded in some cases. In any procedure where the primary aim is palliation, quality of life should be considered, and it can be argued that the dose of opioid is not necessarily the best indicator of a satisfactory result in cordotomy. In a retrospective review, though, it is the best quantifiable variable. In a prospective study other data could have been recorded such as visual analogue pain scales and quality of life assessment with validated questionnaires. It would be reasonable to assume, however, that a treatment producing effective control of previously severe chronic pain, without the detrimental effect of significant side effects, would also lead to a substantial improvement in quality of life. In this series most of the patients who had a documented reduction in opiate dose also had additional positive comments recorded such as "complete relief", "100% better", "pain free", etc, but in the context of this retrospective review these cannot be quantified satisfactorily.

The alternatives to percutaneous cervical cordotomy are not as useful. High doses of opioid in those patients whose pain is partially responsive are associated with significant side effects which may themselves shorten life expectancy. Co-analgesic medication such as non-steroidal anti-inflammatory drugs and drugs affecting pain fibre conduction such as carbamazepine and amitriptyline can be used to treat mesothelioma pain, but in our experience are not very effective. Other techniques to interrupt pain fibres can also be used—for example, intercostal nerve block and intrathecal block—however, most of the patients in this series presented with disease that diffusely affected the hemithorax, making these treatments inappropriate. Palliative radiotherapy was not used in this series for pain control for the same reason. It is our practice, however, to use radiotherapy prophylactically at pleural intubation sites to prevent fistulation of the pleural tumour.<sup>15</sup> One patient in this series underwent limited pleurectomy before referral for cordotomy but none of the other patients in this series had treatment that was any more than palliative in the treatment of their pleural malignancy. The published success rate for percutaneous cervical cordotomy in the control of pain from both benign and malignant causes is 76–89%.<sup>9 16–18</sup> Unsuccessful cordotomy results from the anatomical variations encountered.

Eighteen patients (34%) went on to develop a recurrence of severe pain requiring a subsequent increase in opioid dose, but this was often after a useful period of good pain control. The recurrence of pain was due to further spread into the mediastinum or peritoneum.

There have been a number of staging classifications described for pleural mesothelioma, although none is definitive. All the patients in this series had pain secondary to chest wall invasion, putting them into stage 2 or above of the commonly used classification by Butchart,<sup>19</sup> or stage 4 of a recently proposed

system based on the TNM classification.<sup>20</sup> Staging was performed with the aid of information from plain chest radiographs in all patients, thoracoscopy in 32 patients (60%), and computed tomographic (CT) scans of the thorax in 19 patients (36%). The latter investigation, however, should not be regarded as a definitive assessment in these circumstances as it is known to give a significant rate of false negatives in detecting chest wall invasion in this disease.<sup>21 22</sup> For those patients early in the series, before CT scanning became part of the routine management of pleural mesothelioma, and for those patients where CT scanning could not confirm chest wall invasion, the diagnosis was made at the onset of severe intractable pain typical of chest wall involvement, bearing in mind the natural history of this disease. It is important, however, not to confuse this pain with the dragging discomfort of bulky tumour confined to the parietal pleura without chest wall invasion.

This study has highlighted the low rate of complications that we have observed with this procedure. The incidence of troublesome dysaesthesia was similar to previous studies<sup>7 8 16</sup> and there was no case of severe motor weakness or sphincter disturbance. Thermoanaesthesia frequently occurs following cervical cordotomy, and all patients are warned about this and advised appropriately. Horner's syndrome often occurs<sup>9 16</sup> but gradually becomes less obvious and is not troublesome.

The published mortality at one week for percutaneous cervical cordotomy carried out for all causes of persistent pain (both benign and malignant) is 1–6%.<sup>9</sup> When only those with malignant disease are considered, the reported mortality at one week is 6%.<sup>16</sup> Considering that all of the patients in this series had mesothelioma, some with advanced disease, our results are comparable.

The dose of morphine, time from diagnosis to procedure, and age of the patients who died early within two weeks of the procedure (median 120 mg, 26 weeks, and 58 years, respectively) did not differ significantly from the remainder of the patients in the series. However, this group of patients did have advanced disease and were probably less able to tolerate percutaneous cervical cordotomy as a result, as the procedure may worsen respiratory failure in susceptible individuals or in those on opioids by causing respiratory depression. In the upper cervical region there are ascending and descending respiratory reticular fibres<sup>13 14 23</sup> close to the region where the upper cervical nociceptive fibres lie and, if a high level of analgesia is required (as in pleural mesothelioma), then these fibres may be damaged. If the patient has little reserve in the unaffected lung then a unilateral cordotomy, carried out contralateral to the pain, may temporarily reduce respiration to a life threatening degree.<sup>24</sup> This matter is the subject of an ongoing study in this unit. With tighter patient selection the early mortality in this series could be improved, however, and these results support the use of percutaneous cervical cordotomy for the control of otherwise intractable pain which often

occurs at or soon after presentation in malignant mesothelioma, before the patient enters the terminal stages of their illness. It is the practice of this unit to offer cordotomy to patients when pain due to chest wall involvement, the "costopleural syndrome", is first suspected.

In conclusion, high percutaneous cervical cordotomy is successful in controlling the pain from malignant pleural mesothelioma as assessed by a reduction in opioid dose. There is a low rate of significant complications in this series. Percutaneous cervical cordotomy should be considered in patients with pleural mesothelioma as soon as pain due to chest wall invasion is suspected.

Conflict of interest: none.

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